European Patent Office

SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 99 93 3855

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	JOHNSON P J ET AL: "OVEREXPRESSED PP-60C-SRC CAN INDUCE FOCUS FORMATION WITHOUT COMPLETE TRANSFORMATION OF NIH-3T3 CELLS" MOLECULAR AND CELLULAR BIOLOGY, vol. 5, no. 5, 1985, pages 1073-1083, XP009000334 ISSN: 0270-7306 * the whole document * ---	1,2, 9-11,17	A61K48/00 A01N63/00 C12N15/63 C12N15/85 C12N15/86 C07H21/04
X	BACUS S S ET AL: "TUMOR-INHIBITORY MONOCLONAL ANTIBODIES TO THE HER-2/NEU RECEPTOR INDUCE DIFFERENTIATION OF HUMAN BREAST CANCER CELLS" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 52, 1 May 1992 (1992-05-01), pages 2580-2589, XP000919492 ISSN: 0008-5472 * the whole document * ---	1,2, 9-11,17	
X	ZHU DAN ET AL: "Overexpression of CD44 in p185-neu-transfected NIH3T3 cells promotes an up-regulation of hyaluronic acid-mediated membrane-cytoskeleton interaction and cell adhesion." ONCOGENE, vol. 12, no. 11, 1996, pages 2309-2314, XP009000333 ISSN: 0950-9232 * the whole document * ---	1,2, 9-11,17	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C12N
Y	WO 97 25860 A (HALPERN MICHAEL S ;ENGLAND JAMES M (US); ALLEGHENY UNIVERSITY OF T) 24 July 1997 (1997-07-24) * the whole document * ---	1-20	
	-/--		

The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
MUNICH	8 November 2002	Morawetz, R

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

2

EPO FORM 1503 03.82 (P04C04)

European Patent Office

SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 99 93 3855

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	WO 95 31107 A (UNIV ILLINOIS) 23 November 1995 (1995-11-23) * the whole document * ---	1-20	
D,Y	HUANG A Y C ET AL: "ROLE OF BONE MARROW-DERIVED CELLS IN PRESENTING MHC CLASS I-RESTRICTED TUMOR ANTIGENS" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 264, 13 May 1994 (1994-05-13), pages 961-965, XP002037401 ISSN: 0036-8075 * page 964, left-hand column, paragraph 2 - middle column, paragraph 3 * -----	1-20	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)

The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
MUNICH	8 November 2002	Morawetz, R

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C04)

The examination is being carried out on the **following application documents**:

Text for the Contracting States:
AT BE CH LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Description, pages:

1-54 as published

Claims, No.:

1-20 as received on 23.02.2001 with letter of 22.02.2001

Drawings, sheets:

1/3-3/3 as published

1. Cited documents

The following documents cited in the Supplementary European Search Report are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D2: JOHNSON P J ET AL: 'OVEREXPRESSED PP-60C-SRC CAN INDUCE FOCUS FORMATION WITHOUT COMPLETE TRANSFORMATION OF NIH-3T3 CELLS' MOLECULAR AND CELLULAR BIOLOGY, vol. 5, no. 5, 1985, pages 1073-1083, XP009000334 ISSN: 0270-7306

D3: BACUS S S ET AL: 'TUMOR-INHIBITORY MONOCLONAL ANTIBODIES TO THE HER-2/NEU RECEPTOR INDUCE DIFFERENTIATION OF HUMAN BREAST CANCER CELLS' CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 52, 1 May 1992 (1992-05-01), pages 2580-2589, XP000919492 ISSN: 0008-5472

D4: ZHU DAN ET AL: 'Overexpression of CD44 in p185-neu-transfected NIH3T3 cells promotes an up-regulation of hyaluronic acid-mediated membrane-

cytoskeleton interaction and cell adhesion.' ONCOGENE, vol. 12, no. 11, 1996, pages 2309-2314, XP009000333 ISSN: 0950-9232

D5: WO 97 25860 A (HALPERN MICHAEL S ;ENGLAND JAMES M (US); ALLEGHENY UNIVERSITY OF T) 24 July 1997 (1997-07-24)

D6: WO 95 31107 A (UNIV ILLINOIS) 23 November 1995 (1995-11-23)

D7: HUANG A Y C ET AL: 'ROLE OF BONE MARROW-DERIVED CELLS IN PRESENTING MHC CLASS I-RESTRICTED TUMOR ANTIGENS' SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 264, 13 May 1994 (1994-05-13), pages 961-965, XP002037401 ISSN: 0036-8075

2. Note has been taken of the International Preliminary Examination Report, drawn up for the present application in accordance with the PCT.

3. Article 123(2) EPC

3.1. The amendments filed with the letter dated 22.02.2001 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 123(2) EPC. The amendments concerned are the following:

Claim 8 is based on original claim 8 which referred merely to claim 1 and not to "any preceding claim". The reference to any preceding claim is considered to create new subject-matter for which no basis could be found by the Examining Division.

The same objection applies mutatis mutandis to claims 9, 12, 17, and 18.

3.2. The applicant is kindly invited to indicate the basis for these amendments or to delete them.

4. Subject-matter of the application

The present application relates to cellular immunogens comprising allogeneic donor cells transfected with a transgene cognate (=functionally and evolutionary related between species) to the target proto-oncogene, which transgene encodes

a gene product which induces host immunoreactivity to host self-determinants of the product of the target proto-oncogene. The cognate gene may comprise a wild-type or mutant cognate retroviral oncogene or a wild-type or mutant proto-oncogene of a species different from the host species. The cellular immunogen is prepared from cells obtained from a donor other than the patient and hence allogeneic. The vaccination strategy of the present invention relies on the induction of an immune response that targets tumor cells by virtue of the recognition of the proto-oncogene-specific antigenicity.

5. Articles 83 and 84 EPC

5.1. It is an accepted principle of the case law that, for the purpose of patent protection of a medical application of a substance, a pharmacological effect or any other effect such as an effect observed either in vitro or on animal models is considered to provide sufficient evidence of a therapeutic application if for the skilled person this observed effect directly and unambiguously reflects such a therapeutic application (cf T158/96, T241/95, OJ EPO 2001, 103, T1045/98).

Present claims 19 and 20 relate to the cellular immunogens according to any of claims 1-9 for use in medicine or in the preparation of an anti-cancer vaccine, respectively.
The only pharmacological effect disclosed in present application relates to the immunization of chickens against c-src(527)-induced tumors by vaccination with v-src DNA. In other words, not a cellular immunogen comprising allogeneic donor cells but plasmid DNA has been used for vaccination.

In the present case, in the absence of any data whatsoever which would support a pharmacological effect of the cellular immunogen, a therapeutic application of said cellular immunogen is not sufficiently disclosed.

5.2. The Examining Division is thus of the opinion that the subject-matter of claims 19 and 20 is not sufficiently disclosed in the description to allow the person skilled in the art to perform the invention as claimed (Article 83 EPC) and consequently these claims are also not supported by the description (Article 84 EPC).

6. Article 54 EPC

The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1-20 is not new in the sense of Article 54(1) and (2) EPC.

6.1. D5 discloses (page 10, line 20 - page 11, line 11, claims) a cellular immunogen for immunizing a host against the effects of the product of a target proto-oncogene, the overexpression of which target proto-oncogene is associated with a cancer, which cellular immunogen comprises host cells which have been transfected with at least one transgene construct comprising at least one transgene cognate to the target proto-oncogene and a strong promoter to drive the expression of the transgene in the transfected cells, the transgene encoding a gene product which induces host immunoreactivity to host self-determinants of the product of the target proto-oncogene.

Although the cellular immunogen according to claim 1 of D5 comprises host cells whereas the cellular immunogen according to present claim 1 comprises allogeneic donor cells, this feature is not considered to impart novelty to claim 1 since this feature becomes only technically relevant in combination with the host, i.e. once the host is defined and the cellular immunogen is actually used for immunization. Claim 1 relates however to the cellular immunogen as such, which can not be distinguished from the prior art cellular immunogen. Please note that a cellular immunogen which is syngeneic for one host is allogeneic for all other hosts.
D5 moreover discloses methods for preparing the cellular immunogen and its medical use as an anti-cancer vaccine and thus anticipates the subject-matter of claims 1-20.

6.2. D2 discloses (abstract) that NIH 3T3 cells (murine fibroblasts, allogeneic for e.g. C57BL6 mice) were transfected with plasmids containing Moloney murine leukemia virus long terminal repeats and either chicken c-src or v-src genes. These cells are considered to represent cellular immunogens which fall within the scope of present claims 1, 2, 8-11, 17, and 18. The subject-matter of claim 1, 2, 8-11, 17, and 18 is therefore not new (Article 54(1) and (2) EPC).

6.3. D3 discloses (abstract) hHER-2/neu protooncogene (also called erbB-2) transfected fibroblasts and injection thereof into CD-1/nude mice (allogeneic) and thus also anticipates the subject-matter of claims 1, 2, 8-11, 17, and 18.

6.4. D4 discloses a mouse fibroblast cell line transfected with the $p185^{neu}$ oncogene cDNA which is likewise considered to anticipate the subject-matter of claims 1, 2, 8-11, 17, and 18.

7. Article 56 EPC

Notwithstanding the objections raised above, the Examining Division is of the opinion that the present application lacks an inventive step for the reasons set out below.

Document D5 which is considered to represent the most relevant state of the art, discloses (page 10, line 20 - page 11, line 11, claims) a vaccination strategy based on a cellular immunogen for immunizing a host against the effects of the product of a target proto-oncogene, the overexpression of which target proto-oncogene is associated with a cancer, which cellular immunogen comprises host cells which have been transfected with at least one transgene construct comprising at least one transgene cognate to the target proto-oncogene.

Present application relates to vaccination strategies employing cellular immunogens based on allogeneic donor cells.

Since no particular technical effect has been shown to be linked to the use of allogeneic donor cells, the objective technical problem to be solved by the present invention can merely be seen in the provision of an alternative vaccination strategy.

This is in accordance with the board's case law that any alleged but not supported advantages cannot be taken into account in determining the problem underlying the invention and therefore in assessing inventive step (see T20/81, OJ 1982, 217, point 8 of the reasons; T1051/97).